**Supplementary Figure 1. IL-21 promotes the differentiation of CD4+ T cells that produce IL-22 but not IL-17.** (**a**) Naïve WT CD4+ T cells were stimulated *in vitro* with antibodies to CD3 and CD28 in the presence of IL-21 or IL-6 and anti-TGFβ1 blocking antibody, and the production of IL-22 and IL-17 was measured by ELISA in culture supernatants. (**b**) Effects of IL-6 and anti-TGFβ1 blocking antibody on the expression of *il21*. (**c**) Naïve CD4+ T cells were initially activated in the presence of IL-21, rested, and reactivated in the presence of IL-21, IL-6 and TGFβ1 or TGFβ1, and the expression of
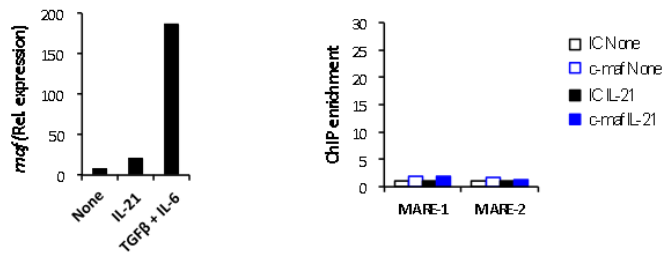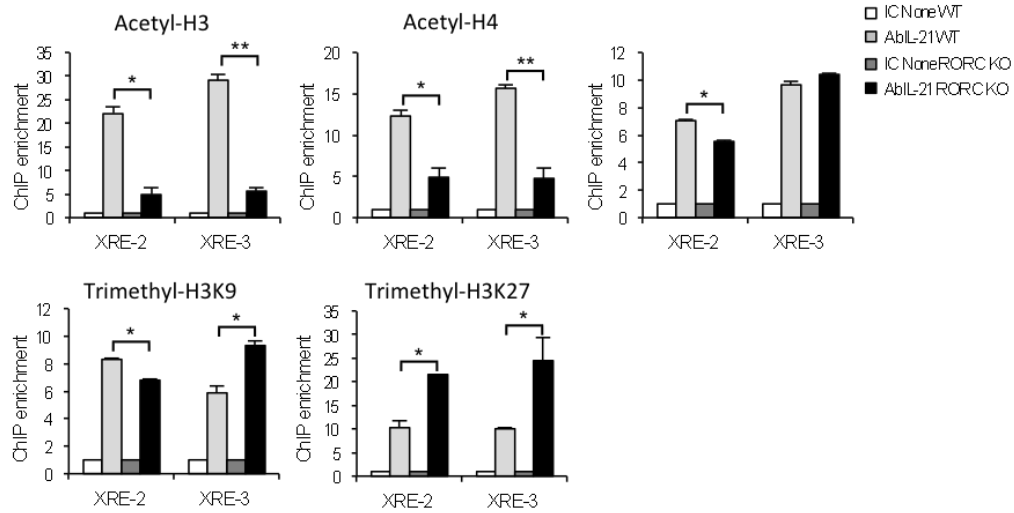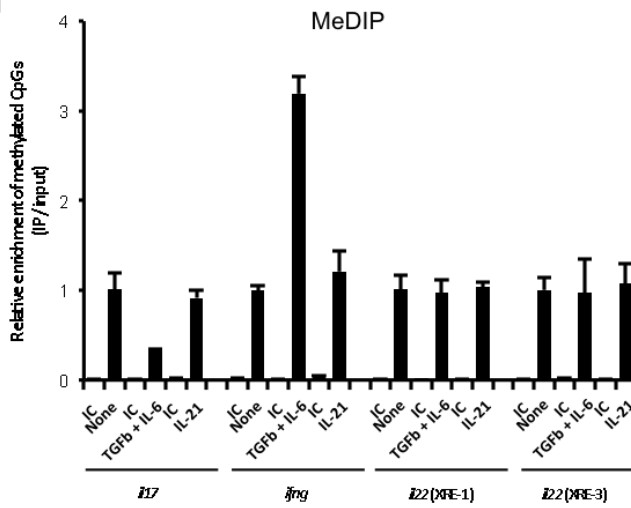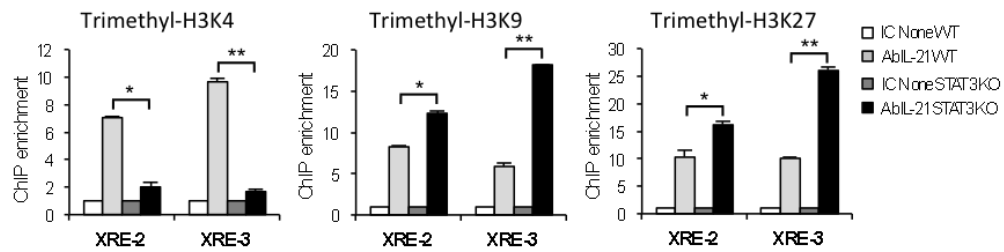
IL-17 and IL-22 was analyzed by flow cytometry. (**d**) Effects of IL-6 and anti-TGFβ1 blocking antibody on the expression of *il21r*, *il23r* and *il1r*. mRNA expression is shown relative to the expression of *gapdh*. * $P < 0.05$ (one-way ANOVA). Results are representative of 3-5 independent experiments.
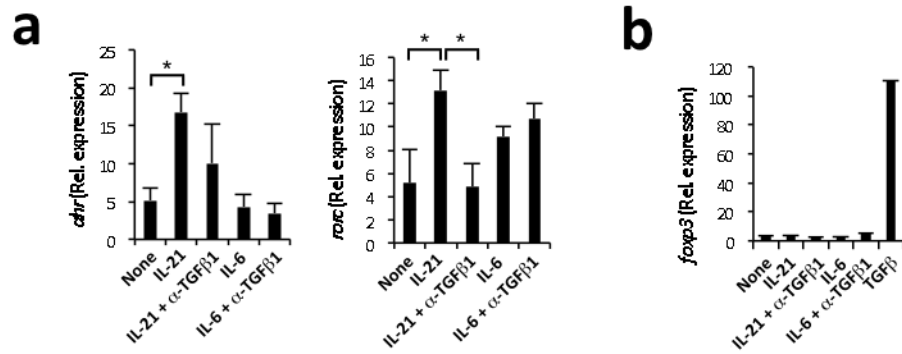
Supplementary Figure 2. Expression of *ahr*, *rorc* and *foxp3* in IL-21-stimulated CD4+ T cells. (a,b) Naïve WT CD4+ T cells were stimulated *in vitro* with antibodies to CD3 and CD28 in the presence of IL-21 or IL-6 and anti-TGFβ1 blocking antibody, and the expression of *ahr*, *rorc* (**a**) and *foxp3* (**b**) was analyzed by qPCR. mRNA expression is shown relative to the expression of *gapdh*. Results are representative of 3-5 independent experiments. * $P < 0.05$ (one-way ANOVA).
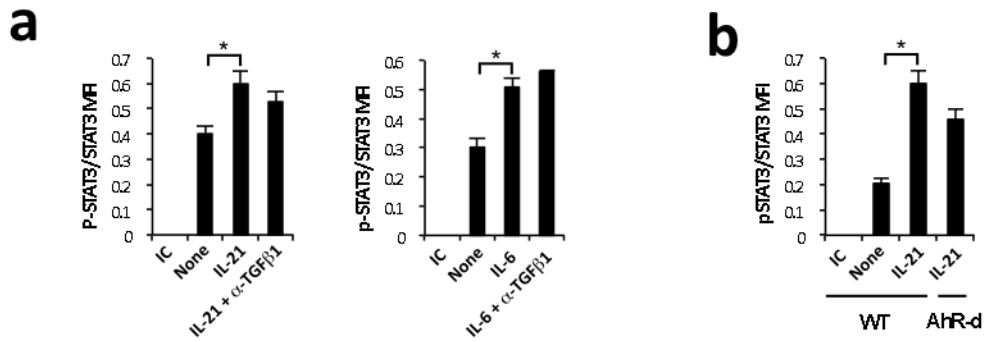
Supplementary Figure 3. STAT3 controls the production of IL-22 by CD4+ T cells stimulated with IL-21. (**a**) Naïve WT CD4+ T cells were stimulated *in vitro* with antibodies to CD3 and CD28 in the presence of IL-21 and anti-TGFβ1 blocking antibody, and the phosphorylation of STAT3 was analyzed by FACS. MFI of phosphorylated STAT3 normalized to total STAT3. (**b**) FACS analysis of phosphorylated STAT3 in WT and AhR-d cells activated in the presence of IL-21. Results are representative of 2-3 independent experiments. * *P* < 0.05 (one-way ANOVA).

a

c
Acetyl-H3

Acetyl-H4

Trimethyl-H3K9

Trimethyl-H3K27

d
MeDIP

e
Trimethyl-H3K4

Trimethyl-H3K9

Trimethyl-H3K27

Supplementary Figure 4. Regulation of *il22* promoter transactivation in IL-21-stimulated CD4+ T cells. Naïve CD4+ T cells were stimulated *in vitro* with antibodies to CD3 and CD28 in the presence of IL-21 or IL-6 and TGFβ1. (**a**) *maf* expression analyzed by qPCR. mRNA expression is shown relative to the expression of *gapdh*. (**b**) ChIP analysis of c-maf interaction with the *il22* promoter. (**c**) Analysis of the epigenetic status of XRE-2 and XRE-3 sites in the *il22* promoter in WT and RORγt-deficient T cells activated in the presence of IL-21. (**d**) Analysis of the CpG methylation of XRE-2 and XRE-3 sites in the *il22* promoter in WT CD4+ T cells activated in the presence of IL-21 or TGFβ1 and IL-6. (e) ChIP analysis of the epigenetic status of the *il22* promoter in WT and STAT3-deficient CD4+ T cells activated in the presence of IL-21. Results are representative of 2-3 independent experiments. * $P < 0.05$, ** $P < 0.01$ and *** $P < 0.001$ (one-way ANOVA).
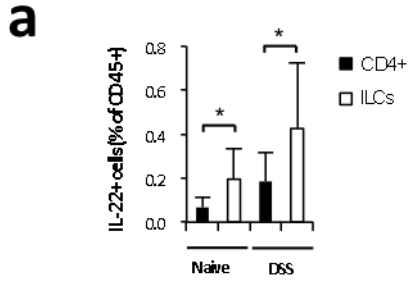
Supplementary Figure 5. IL-22 production by ILCs and CD4+ T cells during DSS-induced colitis. WT mice were given 3 % DSS *ad libitum* in their drinking water and ILCs and CD4+ T cells were analyzed after 7 days of treatment for IL-22 production by flow cytometry. ILCs were defined as CD45+ Lin- Th1.2+. Results are representative of 2 independent experiments. * $P < 0.05$ (Student *t*-test).

Supplementary Table 1: Primers used for ChIP

STAT3	SRE-1	for: 5'-ACGGGAGATCAAAGGCTGCT-3' rev: 5'-GCCAACAAGGTGCTTTTGC-3'
	SRE-2	for: 5'-CTCACCGTGACGTTTTAGGG-3' rev: 5'-GTGAATGATATGACATCAGAC-3'
AhR	XRE-1	for: 5'- ATAGTGCTAATGACTGGAGTCCGCTGC-3' rev: 5'- GTGAGAGGTTGGGGAGTCGATCAAAGA-3'
	XRE-2	for: 5'- ACAGTGATTTTCATGACTTCGCGTTCT-3' rev: 5'- TCCCAGATAGCACCTGACAACTAGACT-3'
	XRE-3	for: 5'- CAATAGCTACGGGAGATCAAAGGCTGC-3' rev: 5'- CTAAAACGTCACGGTGAGGGCCAACAA -3'
c-MAF	MARE-1	for: 5'- GAAGTTGGTGGGAAAATGAGTCCGTGA-3' rev: 5'- GCCATGGCTTTGCCGTAGTAGATTCTG-3'
	MARE-2	for: 5'- CGACGAACATGCTCCCCTGATGTTTTT-3' rev: 5'- AAACTCATAGATTTCTGCAGGACAGCC -3'

Supplementary Table 2: Primers used for *Methyl-DNA immunoprecipitation*

IL-17		for: 5'-AATCACAGCAAAGCATCTCTGTTC-3' rev: 5'-GGTTTTACTACCTCTGTGGTCACT-3'
IFNg		for: 5'-TGAATTCTTAATAATGCTTGTGGTTGG-3' rev: 5'-TGTACCTTGGACCTATACTATGCC-3'
IL-22	XRE-1	for: 5'-ATAGTGCTAATGACTGGAGTCCGCTGC-3' rev: 5'-GTGAGAGGTTGGGGAGTCGATCAAAGA-3'
	XRE-3	for: 5'-CAATAGCTACGGGAGATCAAAGGCTGC-3' rev: 5'-CTAAAACGTCACGGTGAGGGCCAACAA-3'